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## Secondary chemoprophylaxis with isonicotinic acid hydrazide

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*Document Version*

Publisher's PDF, also known as Version of record

*Publication date:*

1968

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Hölscher, C. G. B. (1968). *Secondary chemoprophylaxis with isonicotinic acid hydrazide*. s.n.

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## CHAPTER VI

### CONCLUSIONS AND SUMMARY

#### 1. Conclusions

In the preceeding chapters an attempt was made to valuate the epidemiological situation in the Netherlands.

The arising of contagious sources in a community of which the lower age groups (0-20 years) remain virtually uninfected with tubercle bacilli presents an increasing danger in the future.

This danger is illustrated by a description of an epidemic caused by one source of tuberculous infection in a largely tuberculin negative community of young adults.

As large scale vaccination with BCG was not carried out in the Netherlands the efficacy of the tuberculin test to trace tuberculin-converted contacts is clearly demonstrated.

In this context the merits of chemoprophylaxis with INH are discussed and a review of the most important human and animal trials on chemoprophylaxis with INH is presented.

It is shown that in 1960 a number of uncertainties prevailed to use INH prophylactically on a large scale in the case of recent tuberculin-converted adults.

It was the close observation of this epidemic spread of tuberculous infection among adults which resulted in sufficient material, and in sufficient motives to start the trial which is described in the last chapter.

Secondary prophylaxis with INH proved to offer complete protection against the development of active tuberculosis in young adult tuberculin converters.

During a seven-year follow-up period this rate of protection remained unchanged.

This trial also resulted in some observations concerning the behaviour of the standard Mantoux test of which the most important observation was that INH medication during one year did not affect tuberculin sensitivity expressed by this test.

Close observation of the participants of this trial illicited no toxic effects or important side effects by daily medication with 5-10 mg INH during one year.

## 2. Summary

### *Chapter I*

A review is given of the development of the tuberculosis situation in the Netherlands.

The incidence and prevalence of tuberculosis has decreased to a very low level as a major result of tuberculosis control by tuberculosis clinics, periodical X-ray surveys and adequate treatment of all known cases of active tuberculosis.

Since no systematic BCG vaccination was instituted in the past, the tuberculin test has gained importance in tuberculosis control in the Netherlands, as it is the only way to detect sources of tuberculous infection and those recently infected.

### *Chapter II*

The merits of isonicotinic acid hydrazide (= INH) as a powerful tuberculostatic drug are reviewed.

The effect of prophylactic medication with INH is illustrated by a review of the most important human and animal trials. The different results of these trials suggest differences in materials and methods.

No clear evidence of the effect of secondary prophylaxis with INH in young adults was available in 1960.

### *Chapter III*

An observation of a mass tuberculous infection in a predominantly tuberculin-negative community is described.

The importance of systematic use of the tuberculin test, with the aid of which the development of secondary infection sources was prevented, is shown.

### *Chapter IV*

In this chapter consideration is given to the risks of active tuberculosis in young adults as a result of recent infection by tubercle bacilli.

The necessity to institute prophylactic medication (in 1960) is discussed.

## *Chapter V*

A controlled trial is described in which secondary prophylaxis with INH was used.

In a group of 133 participants who received INH (600 mg daily during 6 months followed by 400 mg during another 6 months) the incidence of active tuberculosis amounted to 0.8% during treatment. During a seven-year follow-up this incidence remained unchanged.

In a group of 128 participants who received a placebo, the incidence was 7% during treatment and 9.4% during the following years.

Some observations concerning the possible influence of INH medication on tuberculin sensitivity, the evaluation of small indurations following conversion, and the relation between the degree of tuberculin sensitivity and tuberculosis incidence, are reported.

No toxic phenomena were observed among 133 participants receiving INH during one year.